FLORIDA CHEMICAL COMPANY, INC.

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December 21, 2004

Ms. Dorothy Shimer
Research Division
Air Resources Board
P.O. Box 2815
Sacramento, California 95812

Dear Ms. Shimer:

This letter is in response to the *Draft (For Peer Review November 2004) Report to the California Legislature, Indoor Air Pollution in California in response to Assembly Bill 1173* and the ARB welcoming of comments on this report.

1. The following appears in the draft language on PAGE 36

"Delfino cites Swedish studies that showed that self-reported asthma prevalence in schoolchildren increased with increasing VOC levels, and asthmatic adult symptoms occurred in association with toluene, C8-aromatics, terpenes, formaldehyde, and Limonene."

We would like this statement to be removed since it is misleading. This statement can only lead to false conclusions regarding terpenes and asthma. Recent scientific research specific to limonene demonstrates that limonene is a prophylactic treatment for asthma[1].

"Examination of the pulmonary function of sensitized rats that inhaled either limonene (unsaturated, ozone scavenger) or eucalyptol (saturated, inert to ozone) showed that limonene inhalation significantly prevents bronchial obstruction while eucalyptol inhalation does not cause any effect." [1]

"In Conclusion, both the pulmonary function tests and pathological data support the hypothesis that the inflammatory cascade of asthmatic events, which may involve a vicious circle of ozone production by white blood cells and recruitment of more such cells, can be intercepted by ozone scavengers. The anti-inflammatory protection provided by limonene to the sensitized animals suggests that a new pharmaceutical paradigm of controlling inflammatory diseases should be seriously considered on the basis of appropriately designed ozone scavengers." [1]

Scientific literature reports that d-Limonene and other terpenes are used to alleviate asthmatic and respiratory symptoms.

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In a multi-centre, randomized, double-blind, placebo-controlled parallel group clinical trial, myrtol standardized (consisting of the monoterpenes d-Limonene, alpha-pinene, and 1,8-cineole) was shown to be a safe and effective alternative to commonly used antibiotics in treating acute bronchitis (Matthys et al., 2000).[2]

1.Keinan E, Alt A, Amir G, Bentur L, Bibi H and Shoseyov D. Natural ozone scavenger prevents asthma in sensitized rats. Bioorganic & Medicinal Chemistry. Currently in Print

2.Matthys, H. et al. 2000. Efficacy and tolerability of myrtol standardized in acute bronchitis. A multi-centre, randomized, double-blined, placebo-controlled parallel group clinical trial vs. cefuroxime and ambroxol. Arzneimittelforschung. 50(8):700-711.

2. The following appears in the draft language on Page 5

"Terpenes, such as pinene and limonene, frequently used in cleaning products for their favorable odor characteristics and solvent properties, react with indoor oxidants to produce formaldehyde and ultrafine PM. Further research is needed to understand the extent and duration of exposure to terpene reaction products, and the potential health effects of those exposures."

We would like the statement changed as follows or removed.

Terpenes, such as pinene and limonene, frequently used in cleaning products for their favorable odor characteristics and solvent properties, **have been shown in laboratory experiments at levels greater than normally observed indoors** to react with indoor oxidants to produce formaldehyde and ultrafine PM. Further research is needed to understand the extent and duration of exposure to terpene reaction products, and the potential health effects of those exposures."

3. The following appears in the draft language on Page 41

"Other chemicals such as isoprene and terpenes, have been shown to react with oxidants, producing irritating products such as formaldehyde, terpene oxides, and fine particles (Long *et al*., 2000; Wilkins *et al*., 2001)."

The Wilkins paper[1] referenced is specific to isoprene, not terpenes. Any data cited from the Long paper should be presented within the context of the research; the terpene based cleaners need to be presented in perspective with other more significant particulate sources. We ask ARB remove the word terpenes or remove the statement altogether.

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The language misrepresents the research to make it appear that terpenes were the subject matter. Isoprene was studied because it is the most abundant biogenic VOC and is a common human respiratory by-product. The word isoprene should be substituted for terpenes to properly portray this research. Another paper[2] by Wilkins does discuss terpenes but the studies were performed at ozone levels of 4 ppm and d-limonene levels of 48 ppm. These are acknowledged by the author as well above any non-industrial exposure levels and were used purely to generate a yes or no answer to whether or not the reactions can occur.

The results of the terpene cleaner data should be presented within the context of all sources of particle generation so the reader isn't selectively biased against terpenes. This study should not be cited, or additional quotes from the research should be added.[3]

The following three references should be added, if the Long[3] paper is to be referenced:

"Windows/doors were opened for approximately ½ hour prior to commencement of terpene experiments in order to increase indoor ozone concentrations with enhanced air exchange." [3]

"Not including data from a scripted mopping event in home SWP2 (11/19/98; 9:20-9:30) where NO particle generation was observed." [3]

"Figure 2 and data from other study homes support previous findings that cooking, cleaning, and many general activities are important sources of particles in indoor residential environments." "On average, the five largest peak $PM_{2.5}$ concentrations were observed during cooking activities…" "The most important indoor sources of coarse-mode peak events were found to be dusting, vigorous walking and sautéing." [3]

1. Wilkins CK, Clausen PA, Wolkoff P, Larsen ST, Hammer M, Larsen K, Hansen V, Nielsen GD. Formation of strong airway irritants in mixtures of isoprene/ozone and isoprene/ozone/nitrogen dioxide. Environmental Health Perspectives 109(9):937-941, 2001.

2. Wilkins CK, Clausen PA, Wolkoff P, Nielsen GD. Chemical and biological evaluation of a reaction mixture of R-(+)-limonene/ozone Formation of strong airway irritants. Enviroment International 26, 511-522, 2001.

3.Christopher M. Long, Helen H Suh, and Petros Koutrakis. Characterization of Indoor Particle Sources Using Continuous Mass and Size Monitors. 2000 Journal of Air & Waste Management Association

4. The following appears in the draft language on Page 41

"They can be airway irritants at concentrations greater than normally encountered in indoor air (Wolkoff *et al*., 2000)".

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We agree with this statement in principal, but not in the context it is used. It should not be used as a segue in an attempt to substantiate irritation claims.

A study conducted by Larsen[1] is the research used by AIHA to establish the WEEL for d-limonene. Larsen determined that limonene is NOT an irritant at the exposure levels found in indoor air. This is supported by the cited Wolkoff research. Both the Larson and Wolkoff studies were authored by the same research team at the National Institute of Occupational Health.

1. ST Larsen, KS Hougaard, M Hammer, Y Alarie, P Wolkoff, PA Clausen, CK Wilkins and GD Nielsen. 2000 *Effects of R and S limonene on the respiratory tract in mice.* Human & Experimental Toxicology.

AIHA, American Industrial Hygienist Association
WEEL, Workplace Environmental Exposure Level
d-Limonene WEEL = 30ppm as an 8 hour time weighted average.

5. The following appears in the draft language on Page 41

"However, terpenes also have been associated with irritation at lower levels: the irritant chemicals are hypothesized to be a product of the reaction of terpenes with oxidants, rather than the terpene (Wilkins *et al*., 2001; Weschler and Shields, 1997).

Again, the Wilkins paper[1] referenced is specific to isoprene, not terpenes. We ask ARB replace the word terpenes with isoprene, or remove the statement altogether.

The language misrepresents the research to make it appear that terpenes were the subject matter. Isoprene was studied because it is the most abundant biogenic VOC and is a common human respiratory by-product. The word isoprene should be substituted for terpenes to properly portray this research. Another paper[2] by Wilkins does discuss terpenes but the studies were performed at ozone levels of 4 ppm and d-Limonene levels of 48 ppm. These are acknowledged by the author as well above any non-industrial exposure levels and were used purely to generate a yes or no answer to whether or not the reactions can occur.

One Weschler study[3] was performed at levels closer to expected ambient conditions but no irritation studies were performed. The study only attempted to monitor hydroxide radical generation from ozone/d-limonene reactions. The authors go on to state the following " we can only speculate on the importance of the OH radical in indoor environments."

The other Weschler citation[4] is a literature review of possible reaction mechanisms and products. The paper simply lists reactions that may be important to indoor air quality; it does not associate terpenes to irritation at low levels since concentration is not discussed.

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1. Wilkins CK, Clausen PA, Wolkoff P, Larsen ST, Hammer M, Larsen K, Hansen V, Nielsen GD. Formation of strong airway irritants in mixtures of isoprene/ozone and isoprene/ozone/nitrogen dioxide. Environmental Health Perspectives 109(9):937-941, 2001.

2. Wilkins CK, Clausen PA, Wolkoff P, Nielsen GD. Chemical and biological evaluation of a reaction mixture of R-(+)-limonene/ozone Formation of strong airway irritants. Environment International 26, 511-522, 2001.

3. Weschler CJ, Shields HC. Measurements of the Hydroxyl Radical in a manipulated but realistic indoor environment. Environ. Sci. Technol. 1997, 31, 3719-3722.

4. Weschler CJ, Shields HC. Potential reactions among indoor pollutants. Atmospheric Environment 31(21), 3487-3495, 1997.

6. The following appears in the draft language Page 42

"Pollutants with reactive double bonds such as terpenes and alkenes react with ozone and nitrogen oxides to produce products that result in airway irritation similar to that of formaldehyde."

This statement is vague and misleading. We ask ARB to remove it, unless it can be substantiated by research demonstrating this at normal ambient concentrations and conditions.

7. The following appears in the draft language on Page 42

"Fan *et al.* (2003) confirmed the reaction of ozone with d-limonene and ozone with α -pinene under indoor conditions to generate submicron particles and other potentially irritating species, such as aldehydes and organic acids."

This statement alone is extremely MISLEADING to the true content of the research. The word condition could be misunderstood to imply typical indoor concentrations as opposed to temperature, pressure, humidity etc.

The author states, "although the compounds present in the mixture are among some of the more commonly observed compounds in indoor air, the concentrations employed in this study tend to be much higher than those observed in nonindustrial indoor environments" [1]

The clear conclusion that can be drawn from the work of Fan et al, is that indoor chemical reactions between ozone and VOC's are OZONE LIMITED. As demonstrated by Fan's VOC study, no reactions/particulate formation occurred with the 23 VOCs studied in the absence of

ozone. Removing specific VOC's from indoor air solves nothing because there is abundant biogenic VOC's (specifically terpenes) in indoor air. This is due to the fact that both humans and plant life emit isoprene and other VOC's. Therefore as long as the elevated ozone levels are present the reactions will occur that generates particulate and irritants. Fan states it best in his conclusion, "…it is even more crucial to reduce outdoor ozone levels".

8. The following appears in the draft language on Page 42

"To minimize these reactions, Fan *et al.* (2003) suggest "limiting use of products that emit high-reactivity alkenes during episodes when outdoor ozone levels are elevated", reducing outdoor ozone levels, and minimizing the penetration of ozone from outdoors."

This research is incorrectly quoted, the author is paraphrased within quote marks. This report should be quoted correctly.

"It is prudent to limit the use of products that emit high-reactivity alkenes during episodes when outdoor O3 levels are elevated. However, given the practical difficulties associated with such changes in established use patterns, it is even more crucial to reduce outdoor O3 levels or to minimize the unimpeded penetration of O3 from outdoors."[1]

1. Fan Z, Lioy P, Weschler C, Fiedler N, Kipen H, and Zhang J, 2003. Ozone-initiated reactions with mixtures of volatile organic compounds under simulated indoor conditions. *Environmental Science and Technology* 37:1811-1827.

9. The following appears in the draft language Page 41 and 42:

"In this growing area of research, investigators have identified an increase in fine particles associated with mopping floors with a pine-scented cleaning product. It is hypothesized that the generation of particles was the result of ambient ozone (up to 48 ppb) reacting with the terpenes in the cleaning product (Long *et al*., 2000). This area of research warrants increased effort in order to understand the association between indoor air pollutants and related health effects."

The results of the terpene cleaner data should be presented within the context of all sources of particle generation so the reader isn't selectively biased against terpenes. This study should not be cited, or additional quotes from the research should be added.

The following three references should be added, if the Long paper is to be referenced:

"Windows/doors were opened for approximately ½ hour prior to commencement of terpene experiments in order to increase indoor ozone concentrations with enhanced air exchange." [1]

"Not including data from a scripted mopping event in home SWP2 (11/19/98; 9:20-9:30) where NO particle generation was observed." [1]

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"Figure 2 and data from other study homes support previous findings that cooking, cleaning, and many general activities are important sources of particles in indoor residential environments." "On average, the five largest peak $PM_{2.5}$ concentrations were observed during cooking activities…" "The most important indoor sources of coarse-mode peak events were found to be dusting, vigorous walking and sautéing." [1]

If the Long et al, 2000 research is cited, the terpene based cleaners need to be presented in perspective with other more significant particulate sources.[1]

1. Christopher M. Long, Helen H Suh, and Petros Koutrakis. Characterization of Indoor Particle Sources Using Continuous Mass and Size Monitors. 2000 Journal of Air & Waste Management Association

We appreciate this opportunity to review the Draft Report and provide our comments. We believe we have outlined suggestions to make significant improvements in this report. These changes are needed to give an accurate and balanced scientific representation of d-limonene and citrus terpenes in relation to indoor air quality. If you have questions, please contact us at 863-294-8483.

Respectfully submitted,

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cc: Jim Mattesich, Livingston and Mattesich